Supporting Information

Application of a High-Throughput Enantiomeric Excess Optical Assay Involving a Dynamic Covalent Assembly: Parallel Enantiomeric Allylation and *Ee* Sensing of Homoallylic Alcohols †

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General Information:

NMR spectra were recorded on Agilent MR 400 at The University of Texas at Austin NMR facility. ESI-mass spectra were obtained on Agilent 6100 at The University of Texas at Austin mass spectrometry facility. Circular dichroism (CD) spectra were recorded on a Jasco J-815 spectropolarimeter at The University of Texas facility. High performance liquid chromatography (HPLC) analysis was performed with OD-H column from Chiralcel.

Experimental Procedures:

Preparation of pre-catalysts



Sheme S2. Synthesis of pre-catalysts with various phospho ligands

A pressure tube equipped with a magnetic stirbar was charged with $[Ir(cod)Cl]_2$ (161.9 mg, 0.24 mmol, 100 mol%), phospho ligand (0.48 mmol, 200mol%), Cs_2CO_3 (312.9 mg, 0.96 mmol, 400 mol%) and 4-Cl-3-NO₂BzOH (192.5 mg, 0.96 mmol, 400 mol%). The tube was purged with argon and an outlet for 5 minutes, followed by the addition of allyl acetate (142µL, 1.2 mmol, 500 mol%) in THF (5.2 mL, 0.05 M). The mixture was stirred for 30 min at room temperature under argon. The reaction mixture was then stirred for 90 min at 80 °C. Upon cooling to ambient temperature, the reaction mixture was diluted and rinsed with CH_2Cl_2 and concentrated in vacuo at ambient temperature. The compound was purified by flash chromatography (SiO₂, 20% Et₂OAc/CH₂Cl₂) and concentrated in vacuo at ambient temperature. The light brown gum was dissolved in small amount of THF and precipitated upon rapid addition of HPLC grade hexanes. Gravity filtration, followed by removal of trace solvents with flushing N₂ gives a yellow powder.

| Pre-catalyst | Phospho ligand | Acid | Vield (%) |
|---------------------------------|---------------------------------|---|-----------|
| (R)-C1 | (R)-BINAP | 4-Cl-3-NO ₂ BzOH | 80 |
| (\mathbf{R}) - \mathbf{C}^2 | $(\mathbf{R}) - \mathbf{BINAP}$ | $4 \text{ CN}_3 \text{ NO}_2 \text{BzOH}$ | 78 |
| (R) - C3 | $(\mathbf{R}) - \mathbf{BINAP}$ | $4 \text{ OH} - 3 \text{ NO}_2 \text{BZOH}$ | 66 |
| (\mathbf{R}) -C4 | (R)-SEGPHOS | 4-Cl-3-NO ₂ BzOH | 76 |
| (R)-C5 | (R)-SEGPHOS | $4 \text{ CN}_3 \text{ NO}_2 \text{BzOH}$ | 83 |
| (R)-C6 | (R)-SYNPHOS | $4-Cl-3-NO_2BZOH$ | 76 |
| (R)-C7 | (R)-SYNPHOS | $4-CN-3-NO_2BZOH$ | 78 79 |
| (R)-C8 | (R)-C1 MeO-BIPHEP | $4-Cl-3-NO_2BZOH$ | 79 |
| (R)-C9 | (R)-Cl MeO-BIPHEP | $4-CN-3-NO_2BzOH$ | 81 |
| (S)-C1 | (S)-BINAP | 4-Cl-3-NO ₂ BzOH | 81 |
| (S)-C2 | (S)-BINAP | 4-CN-3-NO ₂ BzOH | 80 |
| (S)-C3 | (S)-BINAP | 4-OH-3-NO ₂ BzOH | 65 |
| (S)-C4 | (S)-SEGPHOS | 4-Cl-3-NO ₂ BzOH | 76 |
| (S)-C5 | (S)-SEGPHOS | 4-CN-3-NO ₂ BzOH | 80 |
| (S)-C6 | (S)-SYNPHOS | 4-Cl-3-NO ₂ BzOH | 78 |
| (S)-C7 | (S)-SYNPHOS | 4-CN-3-NO ₂ BzOH | 78 |
| (S)-C8 | (S)-Cl, MeO-BIPHEP | 4-Cl-3-NO ₂ BzOH | 80 |
| (S)-C9 | (S)-Cl, MeO-BIPHEP | 4-CN-3-NO ₂ BzOH | 82 |

 Table S3. List of pre-catalyst generated and the yield

General Procedures for Synthesis of 1-Phenylbut-3-en-1-ol (1)

To a vial in the mini-block, pre-catalyst (8.75 μ mol, 5 mol%) and stock solutions of benzyl alcohol (17.5 μ mol, 100 mol%), base (10.5 μ mol, 6 mol%) in THF (0.4 M) and H₂O (0.35 mmol, 200 mol%) was placed. The stock solution of allyl acetate (0.35 mmol, 200 mol%) in THF was added in the mixture and was allowed to stir at 100 °C for 48 hr, at which point the reaction mixture was evaporated onto silica gel using Genevac. Purification of the product by mini-plug silica column chromatography on 96-well filter plate (SiO₂: ethyl acetate:hexanes, 1:50 to 1:20) provided **1** as a colorless oil. Spectroscopic properties matched those in the literature^{11,12}.

HPLC: (Chiralcel OD-H column, hexanes:i-PrOH = 95:5, 0.5 mL/min, 254 nm), (R)-1-Phenylbut-3-en-1-ol: 17.2 min, (S)-1-Phenylbut-3-en-1-ol: 15.2 min.

General Procedures for Multi-component Assembly

All assembly reactions were performed using stock solution of each component *in situ* in acetonitrile without isolation and purification. Pyridine-2-carboxyaldehyde (**2-PA**, 35 mM, 0.0175 mmol, 1 equiv.), zinc triflate ($Zn(OTf)_2$, 35 mM, 0.0175 mmol, 1 equiv.), di-(2-picolyl)amine (**DPA**, 42mM, 0.021 mmol, 1.2 equiv.), 1-phenylbut-3-en-1-ol (**1**, equivalents varies within allylation reactions performed.), and 4-(2-chloroethyl)morpholine hydrochloride (CEM-HCl, 35 mM, 0.0175 mmol, 1 equiv.) were stirred together in acetonitrile in the presence of 3Å activated molecular sieves. The mixture was stirred at room temperature.

General Procedures for TLC Analysis

Each reaction was spotted onto TLC silica plate and developed with 10% ethylacetate in hexane. The TLC plate was placed inside the box that has UV lamp attached and the photo was taken using iphone. It is important in each time, the TLC plate to be placed at the same position and that a picture of blank TLC plate need to taken before the development. The pictures were converted to grey-scale using any kind of photo management software, then using a software Igor pro, the intensity for each spot was counted and the ratio between the starting alcohol and the product alcohol was calculated as percentile.



Tables of ee and % yield of 1 for each reaction

Allylation was performed for each pre-catalyst varying allyl moiety, base and solvent to give product alcohol **1** followed by multi-component assembly. The *ee* obtained from a CD based calibration curve and yield estimated using the TLC method for each condition are shown below. Some of the reactions were randomly selected to compare with HPLC *ee* and isolated yield. When using enantiomers of the pre-catalysts, essentially the opposite *ee* were obtained with slight fluctuations in yield.

| Pre- | Allyl | Base | Solvent | CD ee | HPLC | TLC yield | Isolated |
|----------|--------|--------------------------------|---------|-------|------|-----------|-----------|
| catalyst | Moiety | | | | ee | (%) | yield (%) |
| (R)-C1 | 1a | Cs_2CO_3 | THF | 90 | 92 | 80 | 85 |
| | | | MeCN | 8 | 54 | 25 | 18 |
| | | | Dioxane | 88 | 90 | 68 | 52 |
| | | K_2CO_3 | THF | 45 | 77 | 48 | 58 |
| | | | MeCN | 11 | 47 | 15 | 12 |
| | | | Dioxane | 65 | 68 | 32 | 25 |
| | | K_3PO_4 | THF | 85 | 90 | 80 | 80 |
| | | | MeCN | 12 | 48 | 25 | 23 |
| | | | Dioxane | 88 | 89 | 83 | 78 |
| | | strycine | THF | 18 | 51 | 22 | 43 |
| | | | MeCN | 7 | 42 | 16 | 12 |
| | | | Dioxane | 12 | 38 | 33 | 48 |
| (R)-C2 | 1a | Cs_2CO_3 | THF | 94 | 98 | 85 | 84 |
| | 1b | | | 90 | 94 | 85 | - |
| | 1a | K_3PO_4 | | 90 | 84 | 80 | - |
| (R)-C4 | 1a | Cs_2CO_3 | | 88 | 93 | 75 | 80 |
| | 1b | | | 87 | 93 | 78 | 76 |
| (R)-C5 | 1a | Cs_2CO_3 | | 89 | 94 | 80 | 78 |
| | 1b | | | 90 | 94 | 75 | 80 |
| | 1a | K ₃ PO ₄ | | 91 | 96 | 70 | - |
| (R)-C6 | 1a | Cs_2CO_3 | | 86 | 84 | 82 | 77 |
| | 1b | | | 85 | 84 | 77 | - |
| (R)-C8 | 1a | Cs_2CO_3 | | 84 | 86 | 80 | 75 |
| | 1b | | | 84 | 85 | 75 | - |

| Pre-catalyst | Allyl Moiety | Base | Solvent | CD ee | TLC yield (%) |
|--------------|--------------|---------------------------------|---------|-------|---------------|
| (R)-C1 | 1a | Cs ₂ CO ₃ | THF | 90 | 80 |
| | | | MeCN | 8 | 25 |
| | | | Dioxane | 88 | 68 |
| | | K_2CO_3 | THF | 45 | 48 |
| | | | MeCN | 11 | 15 |
| | | | Dioxane | 65 | 32 |

| K ₃ PO ₄ | THF | 85 | 80 |
|--------------------------------|---|--|--|
| | MeCN | 12 | 25 |
| | Dioxane | 88 | 83 |
| strycine | THF | 18 | 22 |
| - | MeCN | 7 | 16 |
| | Dioxane | 12 | 33 |
| Cs_2CO_3 | THF | 93 | 68 |
| | MeCN | 14 | 20 |
| | Dioxane | 90 | 65 |
| K_2CO_3 | THF | 58 | 52 |
| | MeCN | 18 | 24 |
| | Dioxane | 35 | 28 |
| K ₃ PO ₄ | THF | 92 | 80 |
| | MeCN | 20 | 28 |
| | Dioxane | 88 | 64 |
| strycine | THF | 19 | 24 |
| | MeCN | 11 | 25 |
| | Dioxane | 16 | 24 |
| | K ₃ PO ₄ strycine Cs ₂ CO ₃ K ₂ CO ₃ K ₃ PO ₄ strycine | $\begin{array}{ccc} K_3PO_4 & THF & MeCN & \\ & Dioxane & \\ strycine & THF & \\ MeCN & Dioxane & \\ Cs_2CO_3 & THF & \\ MeCN & \\ Dioxane & \\ K_2CO_3 & THF & \\ MeCN & \\ Dioxane & \\ K_3PO_4 & THF & \\ MeCN & \\ Dioxane & \\ strycine & THF & \\ MeCN & \\ Dioxane & \\ Strycine & THF & \\ MeCN & \\ Dioxane & \\ Strycine & THF & \\ MeCN & \\ Dioxane & \\ Strycine & THF & \\ MeCN & \\ Dioxane & \\ Strycine & THF & \\ MeCN & \\ Dioxane & \\ Strycine & THF & \\ MeCN & \\ Strycine & THF & \\ MeCN & \\ Strycine & \\ $ | $\begin{array}{cccccccccccccccccccccccccccccccccccc$ |

| Pre-catalyst | Allyl Moiety | Base | Solvent | CD ee | TLC yield (%) |
|--------------|--------------|---------------------------------|---------|-------|---------------|
| (R)-C2 | 1a | Cs ₂ CO ₃ | THF | 94 | 85 |
| | | | MeCN | 12 | 20 |
| | | | Dioxane | 86 | 65 |
| | | K_2CO_3 | THF | 52 | 61 |
| | | | MeCN | 14 | 10 |
| | | | Dioxane | 68 | 52 |
| | | K ₃ PO ₄ | THF | 90 | 80 |
| | | | MeCN | 21 | 28 |
| | | | Dioxane | 92 | 77 |
| | | strycine | THF | 20 | 25 |
| | | | MeCN | 12 | 14 |
| | | | Dioxane | 12 | 18 |
| | 1b | Cs_2CO_3 | THF | 90 | 85 |
| | | | MeCN | 7 | 12 |
| | | | Dioxane | 90 | 72 |
| | | K_2CO_3 | THF | 33 | 43 |
| | | | MeCN | 7 | 12 |
| | | | Dioxane | 68 | 48 |
| | | K_3PO_4 | THF | 88 | 87 |
| | | | MeCN | 15 | 22 |
| | | | Dioxane | 88 | 75 |
| | | strycine | THF | 18 | 14 |
| | | - | MeCN | 10 | 12 |
| | | | Dioxane | 21 | 34 |

| Pre-catalyst | Allyl Moiety | Base | Solvent | CD ee | TLC yield (%) |
|--------------|--------------|---------------------------------|---------|-------|---------------|
| (R)-C3 | 1a | Cs ₂ CO ₃ | THF | 85 | 74 |
| | | | MeCN | 15 | 22 |
| | | | Dioxane | 78 | 70 |
| | | K_2CO_3 | THF | 65 | 51 |
| | | | MeCN | 14 | 22 |
| | | | Dioxane | 64 | 52 |
| | | K ₃ PO ₄ | THF | 70 | 80 |
| | | | MeCN | 14 | 28 |
| | | | Dioxane | 67 | 58 |
| | | strycine | THF | 15 | 22 |
| | | 2 | MeCN | 8 | 12 |
| | | | Dioxane | 12 | 12 |
| | 1b | Cs ₂ CO ₃ | THF | 87 | 80 |
| | | 2 5 | MeCN | 12 | 19 |
| | | | Dioxane | 87 | 70 |
| | | K ₂ CO ₃ | THF | 49 | 44 |
| | | 2 5 | MeCN | 10 | 18 |
| | | | Dioxane | 69 | 52 |
| | | K ₃ PO ₄ | THF | 80 | 70 |
| | | 5 | MeCN | 14 | 22 |
| | | | Dioxane | 78 | 68 |
| | | strvcine | THF | 11 | 28 |
| | | 5 | MeCN | 6 | 10 |
| | | | Dioxane | 10 | 23 |
| | | | | | |
| Pre-catalyst | Allyl Moiety | Base | Solvent | CD ee | TLC yield (%) |
| (R)-C4 | 1a | Cs_2CO_3 | THF | 88 | 75 |
| | | | MeCN | 12 | 28 |
| | | | Dioxane | 81 | 61 |
| | | K_2CO_3 | THF | 66 | 52 |
| | | | MeCN | 14 | 20 |
| | | | Dioxane | 61 | 44 |
| | | K ₃ PO ₄ | THF | 88 | 80 |
| | | | MeCN | 12 | 22 |
| | | | Dioxane | 75 | 68 |
| | | strycine | THF | 8 | 20 |
| | | | MeCN | 11 | 15 |
| | | | Dioxane | 21 | 28 |
| | 1b | Cs_2CO_3 | THF | 87 | 78 |
| | | | MeCN | 10 | 14 |
| | | | Dioxane | 82 | 70 |
| | | K_2CO_3 | THF | 45 | 50 |
| | | | MeCN | 13 | 22 |
| | | | Dioxane | 78 | 41 |
| | | K ₃ PO ₄ | THF | 87 | 80 |

| | | | MeCN | 12 | 10 |
|--------------|--------------|---------------------------------|----------|-------|---------------|
| | | | Dioxane | 85 | 70 |
| | | strvcine | THF | 22 | 20 |
| | | j- j | MeCN | 12 | 20 |
| | | | Dioxane | 8 | 20 24 |
| | | | Dionuite | 0 | |
| Pre-catalyst | Allyl Moiety | Base | Solvent | CD ee | TLC yield (%) |
| (R)-C5 | 1a | Cs_2CO_3 | THF | 89 | 80 |
| | | | MeCN | 17 | 12 |
| | | | Dioxane | 86 | 64 |
| | | K_2CO_3 | THF | 52 | 48 |
| | | | MeCN | 12 | 20 |
| | | | Dioxane | 60 | 42 |
| | | K ₃ PO ₄ | THF | 91 | 70 |
| | | | MeCN | 15 | 28 |
| | | | Dioxane | 90 | 65 |
| | | strycine | THF | 25 | 24 |
| | | je j | MeCN | 14 | 16 |
| | | | Dioxane | 20 | 28 |
| | 1b | Cs ₂ CO ₃ | THF | 90 | 75 |
| | | 2 3 | MeCN | 15 | 32 |
| | | | Dioxane | 89 | 64 |
| | | K ₂ CO ₃ | THF | 45 | 49 |
| | | 2 5 | MeCN | 14 | 22 |
| | | | Dioxane | 65 | 38 |
| | | K ₃ PO ₄ | THF | 88 | 72 |
| | | 54 | MeCN | 18 | 25 |
| | | | Dioxane | 87 | 68 |
| | | strvcine | THF | 21 | 34 |
| | | ~ | MeCN | 14 | 21 |
| | | | Dioxane | 16 | 28 |
| | | | | | |
| Pre-catalyst | Allyl Moiety | Base | Solvent | CD ee | TLC yield (%) |
| (R)-C6 | 1a | Cs_2CO_3 | THF | 86 | 82 |
| | | | MeCN | 18 | 30 |
| | | | Dioxane | 75 | 62 |
| | | K_2CO_3 | THF | 44 | 51 |
| | | | MeCN | 14 | 12 |
| | | | Dioxane | 60 | 28 |
| | | K_3PO_4 | THF | 85 | 66 |
| | | | MeCN | 10 | 28 |
| | | | Dioxane | 70 | 57 |
| | | strycine | THF | 18 | 11 |
| | | - | MeCN | 12 | 18 |
| | | | Dioxane | 18 | 21 |
| | 1b | Cs_2CO_3 | THF | 85 | 77 |

| | | | MeCN | 18 | 12 |
|--------------|----------------------|--|----------------------------|----------|----------------------|
| | | | Dioxane | 70 | 58 |
| | | K ₂ CO ₂ | THF | 42 | 52 |
| | | 112003 | MeCN | 10 | 18 |
| | | | Diovane | 55 | 10 42 |
| | | K PO | TUE | 93 84 | 42 |
| | | K ₃ FO ₄ | $\frac{1111}{M_{\odot}CN}$ | 04 | 00 16 |
| | | | Discourse | 0 | 10 |
| | | , · | Dioxane | 48 | 55 20 |
| | | strycine | 1 HF | 15 | 20 |
| | | | MeCN | 15 | 21 |
| | | | Dioxane | 18 | 31 |
| | | | 0.1 | | |
| Pre-catalyst | Allyl Moiety | Base | Solvent | CD ee | TLC yield (%) |
| (R)-C7 | 1a | Cs_2CO_3 | THF | 82 | 78 |
| | | | MeCN | 12 | 22 |
| | | | Dioxane | 75 | 64 |
| | | K_2CO_3 | THF | 37 | 61 |
| | | | MeCN | 18 | 15 |
| | | | Dioxane | 55 | 22 |
| | | K ₃ PO ₄ | THF | 74 | 58 |
| | | J - 4 | MeCN | 15 | 22 |
| | | | Dioxane | 77 | 62 |
| | | strucine | THE | 20 | 14 |
| | | stryenie | MeCN | 16 | 14 |
| | | | Diovane | 18 | 25 |
| | 1h | C_{S} | THE | 87 | 80 |
| | 10 | CS_2CO_3 | MaCN | 0 | 14 |
| | | | Diovono | 69 | 1 4 60 |
| | | V CO | | 08 | 54 |
| | | $\mathbf{K}_2\mathbf{CO}_3$ | $\Pi \Gamma$ | 44 | 54 16 |
| | | | Discourse | 11 50 | 10 |
| | | V DO | Dioxane | 59 | 52 |
| | | K_3PO_4 | | /6 | 12 |
| | | | MeCN | 12 | 24 |
| | | | Dioxane | 51 | 58 |
| | | strycine | THF | 18 | 21 |
| | | | MeCN | 6 | 10 |
| | | | Dioxane | 12 | 27 |
| | A 11 - 1 N Z - 1 - 1 | | 0.1 | | TIO 11/20 |
| Pre-catalyst | Allyl Moiety | Base | Solvent | CD ee | TLC yield (%) |
| (R)-C8 | 1a | Cs_2CO_3 | THF | 84 | 80 |
| | | | MeCN | 9 | 11 |
| | | | Dioxane | 61 | 58 |
| | | K_2CO_3 | THF | 46 | 54 |
| | | | MeCN | 17 | 15 |
| | | | Dioxane | 61 | 42 |
| | | K ₃ PO ₄ | THF | 84 | 71 |

| | | | MeCN | 10 | 8 |
|--------------|--------------|---------------------------------|---------|-------|---------------|
| | | | Dioxane | 77 | 59 |
| | | strvcine | THF | 15 | 16 |
| | | 5 | MeCN | 7 | 10 |
| | | | Dioxane | 10 | 12 |
| | 1b | Cs ₂ CO ₃ | THF | 84 | 75 |
| | | 2 5 | MeCN | 11 | 16 |
| | | | Dioxane | 66 | 55 |
| | | K ₂ CO ₃ | THF | 40 | 43 |
| | | 2 5 | MeCN | 12 | 14 |
| | | | Dioxane | 53 | 52 |
| | | K ₃ PO ₄ | THF | 80 | 71 |
| | | J - T | MeCN | 14 | 18 |
| | | | Dioxane | 55 | 52 |
| | | strvcine | THF | 12 | 22 |
| | | 2019 00000 | MeCN | 10 | 14 |
| | | | Dioxane | 12 | 14 |
| | | | | | |
| Pre-catalyst | Allyl Moiety | Base | Solvent | CD ee | TLC yield (%) |
| (R)-C9 | 1a | Cs ₂ CO ₃ | THF | 85 | 82 |
| | | | MeCN | 11 | 8 |
| | | | Dioxane | 62 | 56 |
| | | K_2CO_3 | THF | 40 | 36 |
| | | | MeCN | 16 | 18 |
| | | | Dioxane | 61 | 52 |
| | | K ₃ PO ₄ | THF | 86 | 78 |
| | | | MeCN | 14 | 14 |
| | | | Dioxane | 52 | 55 |
| | | strycine | THF | 10 | 12 |
| | | - | MeCN | 15 | 6 |
| | | | Dioxane | 17 | 15 |
| | 1b | Cs ₂ CO ₃ | THF | 83 | 78 |
| | | | MeCN | 13 | 12 |
| | | | Dioxane | 76 | 55 |
| | | K ₂ CO ₃ | THF | 66 | 48 |
| | | 2 5 | MeCN | 14 | 12 |
| | | | Dioxane | 63 | 38 |
| | | K ₃ PO ₄ | THF | 84 | 75 |
| | | т - ц | MeCN | 12 | 12 |
| | | | Dioxane | 55 | 40 |
| | | strycine | THF | 18 | 27 |
| | | | MeCN | 6 | 9 |
| | | | Dioxane | 11 | 18 |